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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,861	11/14/2003	Jonathan Minden	94363CIPDIVDIV	1855

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,861	MINDEN ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *23-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-37* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/22/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicants' response to the Office Action mailed 19 January 2007 is acknowledged (Paper filed 6/22/07). In the amendment filed therein the specification was modified to correct trademarks. Currently, claims 1-37 are subject to Restriction and Election Requirement. Claims 23-37 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as claims drawn to a non-elected invention. Claims 1-22 are under consideration.

2. Objections and/or rejections of record not reiterated herein have been withdrawn.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the Examiner on form PTO-892 or Applicant on form PTO-1449 has cited the references they have not been considered. (For example, see listing of references).

4. The information disclosure statement (IDS) filed on 6/22/07 has been considered as to the merits.

NEW GROUNDS OF REJECTIONS

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 1-5, 13-15 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldman et al. (European Journal of Biochem., 131 pages 473-480, 1983) in view of Waggoner et al. (U.S. Patent #5,268,486) and further in view of Sargent P.B. (NeuroImage, 1994, Volume 1, Number 4, pages 288-295) and Luby-Phelps et al. (Biophysical Journal, Volume 65, pages 236-242, July 1993).

Goldman et al. teach double-labeled radiography in two-dimensional gel electrophoresis protein gels. Cultures of *E.coli* were labeled with [^{3}H]leucine and [^{14}C]leucine. The samples were mixed and separated on a two dimensional gel. Data from each of the radio-nucleotides were measured with filters.

The measurement of only [^{14}C]leucine was collected photographically from the red-light sensitive layer using a red filter and [^{3}H]leucine was collected from a blue light sensitive layer using a blue filter. Specifically, two cell extracts were grown and labeled. Cells from the two cultures were mixed to give a [^{3}H]leucine to [^{14}C]leucine ratio of 10:1. See page 474 – Labeling of cells at two defined growth rates and preparation of cell extracts. (claim 1 steps a-d). The protein samples were separated by two dimensional gel electrophoresis and the labels were detected. See page 474, 2nd column. (claim 1 step e) Captured images of the detected labels were processed by computer analysis and evaluated for the proteins of interest. The captured images were stored in two files. One file contained data recorded from color negatives through a no.47 blue filter for capturing data from [^{3}H]leucine and form spillover of [^{14}C]leucine. The other file contained data recorded from color negatives through the no.25 red filter and contained special and quantitative data from [^{14}C]leucine. See page 475-478. (claim 1 step f)

Goldman et al. differ from the instant invention in not specifically teaching the use of a set of matched luminescent dyes.

However, Waggoner et al. teach luminescent cyanine dyes that are utilized to quantify a variety of proteins or other materials in a system by labeling all of a mixture of proteins in the system and subsequently separating them by a means. See column 3 lines 38-42.

In another embodiment, the dyes are employed in multi-parameter procedure. A plurality of luminescent cyanine or related dyes are attached to a plurality of different components. The components are separated and identified by their respective tagging dyes. See column 3 line 53 through column 4 line 35.

The cyanine and related dyes of this invention are taught to be especially well adapted for the analysis of a mixture of components wherein a variety of excitation and emission wavelengths are required because specific cyanine and related dyes can be synthesized to have a wide range of specific excitation and emission wavelengths by varying the number of methane groups or by modifying the cyanine ring structure. See column 4 lines 36-45. further, the dyes are disclosed to be photostable and soluble in reaction solutions. See column 6 lines 9-24.

With respect to the limitations recited in claim 1 and claim 13 directed to the net charge, light emitted, and pH of the dyes, these limitations are intrinsic to the composition and as such are encompassed by cyanine dye mixtures in US Patent #5,268,486. Both inventions have the same core cyanine dye structures and as such appear to have the same functional characteristics, absent evidence to the contrary. This is support by the instant disclosure on page 17 section 045, for example. A compound and its properties are inseparable. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963).

It would have been prima facie obvious to one of ordinary skill in the art to utilize the luminescent cyanine dye mixtures taught by Waggoner et al. in the method of Goldman et al. because Waggoner et al. taught that the cyanine and related dyes were especially well adapted for the analysis of a mixture of components wherein a variety of excitation and emission wavelengths are required because specific cyanine and related dyes can be synthesized to have a wide range of specific excitation and emission wavelengths by varying the number of methane groups or by modifying the cyanine ring structure. See column 4 lines 36-45. Further, the dyes are disclosed to be photostable and soluble in reaction solutions. See column 6 lines 9-24.

One of ordinary skill in the art would have been motivated to modify the general formula recited in order to control factors related to dye solubility, reduce nonspecific binding, while monitoring charge to minimally perturb the function of the labeled product.

One of ordinary skill in the art would have been motivated to replace the radioactive labels taught by Goldman et al. with the luminescent dyes taught by Waggoner et al. to eliminate the possible effects generated in the utility of radioactive material.

Goldman et al. in view of Waggoner et al. differ from the instant invention in not specifically teaching the combination of two different luminescent dyes to form a matched set, wherein the net charge, ionic characteristics, and pH characteristics of the combined dyes are matched. In preferred embodiments, the instant specification discloses the combination of Cy3 and Cy5 (for example see description of figures on pages 8 and 9 – see example 1 on page 22 – see protein labeling on page 24 and 25 – see gel imaging on page 26).

Sargent and Luby-Phelps et al. both teach the utility of Cy3 and Cy5 in combination (applicants matched set). Specifically, Sargent employs Cy3 and Cy5 to simultaneously detect pairs of antigens in immunofluorescence techniques. The combination of Cy3 and Cy5 eliminated problems previously seen in amphibian cardiac ganglion analyses. Also the combination of Cy3 and Cy5 was as good or better than the results obtained with FITC and Texas Red See abstract.

While, Luby-Phelps et al. teach that Cy3.18 and Cy5.18 are homologous indocyanine dyes that can used as a ratio pair for fluorometric determination of solvent viscosity. See abstract and page 238. Cy3/Cy5 ration measurements of solvent viscosity is taught to be simple and suitable for a wide variety of applications. See page 240 Discussion.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to take the cyanine dye method taught by Goldman et al. in view of Waggoner and combine them to form a set of matched compositions as taught by Sargent and Luby-Phelps et al. because Sargent and Luby-Phelps et al. taught that this allowed for multiple parameter analysis. See Sargent – abstract and Luby-Phelps et al. page 241, figure 4 for example.

The use of the cyanine dyes disclosed by Waggoner as matched sets (Cy3 and Cy5) in protein analysis as taught by Goldman et al. would have been obvious to one of ordinary skill in the art because Sargent taught that Cy3 and Cy5 eliminated problems previously seen in amphibian cardiac ganglion analyses and were as good or better than the results obtained with FITC and Texas Red See abstract.

While, Luby-Phelps et al. taught that Cy3.18 and Cy5.18 are homologous indocyanine dyes that can used as a ratio pair for fluorometric determination of solvent viscosity further allowing for simple procedures that are suitable for a wide variety of applications. See abstract and page 238 and page 240 Discussion.

One having ordinary skill in the art would have been motivated to combine the two dyes in order to test multiple samples in a single assay thereby reducing assay time and simultaneously produce more data for analysis (single assay with multiple results verses multiple assays showing only a single results.

II. Claims 6 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldman et al. (European Journal of Biochem., 131 pages 473-480, 1983) in view of Waggoner et al. (U.S. Patent #5,268,486) and further in view of Sargent P.B. (NeuroImage, 1994, Volume 1, Number 4, pages 288-295) and Luby-Phelps et al. (Biophysical Journal, Volume 65, pages 236-242, July 1993) as applied to claims 1-5, 13-15 and 22 above, and further in view of Potter (Electrophoresis, 1990, Vol.11, pages 415-419).

Please see Goldman et al. in view of Waggoner et al. and further in view of Sargent P.B. and Luby-Phelps et al. as set forth above.

Goldman et al. in view of Waggoner et al. and further in view of Sargent P.B. and Luby-Phelps et al. differ from the instant invention in not teaching image processing with arithmetic operations and pixel measurments.

However, Potter discloses a CLIP image processing system for the complete analysis of two-dimensional gel electrophoresis images. The CLIP series computers use a processor for every pixel of the camera image so that image processing algorithms run in parallel. The advantage of the CLIP system is it's speed of processing. See abstract and pages 416-417, for example.

It would have been prima facie obvious to one of ordinary skill in the art to utilize image processing with arithmetic operations and pixel measurments (such as CLIP) as taught by Potter in the method of Goldman et al. in view of Waggoner et al. and further in view of Sargent P.B. and Luby-Phelps et al. because Potter taught that the advantage of the CLIP system is it's speed of processing. See abstract and pages 416-417, for example.

III. Claims 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldman et al. (European Journal of Biochem., 131 pages 473-480, 1983) in view of Waggoner et al. (U.S. Patent #5,268,486) and further in view of Sargent P.B. (NeuroImage, 1994, Volume 1, Number 4, pages 288-295) and Luby-Phelps et al. (Biophysical Journal, Volume 65, pages 236-242, July 1993) as applied to claims 1-5, 13-15 and 22 above, and further in view of Anderson et al. (Clinical Chemistry, 1981, Vol.27, No.11, pages 1807-1820).

Please see Goldman et al. in view of Waggoner et al. and further in view of Sargent P.B. and Luby-Phelps et al. as set forth above.

Goldman et al. in view of Waggoner et al. and further in view of Sargent P.B. and Luby-Phelps et al. differ from the instant invention in not specifically teaching image normalization, substration and multiplication in order to analyze two-dimensional gels.

However, Anderson et al. disclose computerized procedures to evaluate two-dimensional gels. The system comprises programs for image acquisition, background subtracting and smooting (normalizing), spot detection, gaussian spot modeling (multiplying), and pattern matching/comparison. See abstract and pages 1810 –1814. Anderson et al. taught that systematic errors exist in gel analyses due to film variation, densitometric noise, and gel varaiation. See page 1815 last line of column 1 through 1st paragraph of column 2.

Anderson et al. also taught that there are various approaches to the anlaysis of two-dimensional gel images. The choice of a particular procedure of analysis depends on the computer and display hardware available, the qulaity of the patterns to be analyzed, and the mathematical or programming strategy preferred. See page 1808-2nd paragraph. The combination of procedures taught by Anderson et al. to analyze gels allowed for the study of gene expression against the background of the real complexity of the cell. See page 1819 – 2nd column, last paragraph.

It would have been prima facie obvious to one of ordinary skill in the art to utilize gel image processing that included normalization, substration and multiplication as taught by Anderson et al. in the method of Goldman et al. in view of Waggoner et al. and further in view of Sargent P.B. and Luby-Phelps et al. because Anderson et al. taught that his combination of procedures allowed for the study of gene expression against the background of the real complexity of the cell. See page 1819 – 2nd column, last paragraph.

Also, it would have been obvious to one having ordinary skill in the art at the time the invention was made to employ various known gel analyses techniques as a means of optimizing the data, since it has been held that the provision of adjustablity, where needed, involves only routine skill in the art. *In re Stevens,* 101 USPQ 284 (CCPA 1954).

IV. Claims 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldman et al. (European Journal of Biochem., 131 pages 473-480, 1983) in view of Waggoner et al. (U.S. Patent #5,268,486) and further in view of Sargent P.B. (NeuroImage, 1994, Volume 1, Number 4, pages 288-295) and Luby-Phelps et al. (Biophysical Journal, Volume 65, pages 236-242, July 1993) and Potter (Electrophoresis, 1990, Vol.11, pages 415-419) as applied to claims 6 and 16 above, and further in view of Anderson et al. (Clinical Chemistry, 1981, Vol.27, No.11, pages 1807-1820).

Please see Goldman et al. in view of Waggoner et al. and further in view of Sargent P.B. and Luby-Phelps et al. and Potter as set forth above.

Goldman et al. in view of Waggoner et al. and further in view of Sargent P.B. and Luby-Phelps et al. and Potter differ from the instant invention in not specifically teaching image normalization, substration and multiplication in order to analyze two-dimensional gels.

However, Anderson et al. disclose computerized procedures to evaluate two-dimensional gels. The system comprises programs for image acquisition, background subtracting and smooting (normalizing), spot detection, gaussian spot modeling (multiplying), and pattern matching/comparison. See abstract and pages 1810 –1814.

Anderson et al. taught that systematic errors exist in gel analyses due to film variation, densitometric noise, and gel varaiation. See page 1815 last line of column 1 through 1st paragraph of column 2.

Anderson et al. also taught that there are various approaches to the anlaysis of two-dimensional gel images. The choice of a particular procedure of analysis depends on the computer and display hardware available, the qulaity of the patterns to be analyzed, and the mathematical or programming strategy preferred. See page 1808-2nd paragraph. The combination of procedures taught by Anderson et al. to analyze gels allowed for the study of gene expression against the background of the real complexity of the cell. See page 1819 – 2nd column, last paragraph.

It would have been prima facie obvious to one of ordinary skill in the art to utilize gel image processing that included normalization, substration and multiplication as taught by Anderson et al. in the method of Goldman et al. in view of Waggoner et al. and further in view of Sargent P.B. and Luby-Phelps et al. and Potter because Anderson et al. taught that his combination of procedures allowed for the study of gene expression against the background of the real complexity of the cell. See page 1819 – 2nd column, last paragraph.

Also, it would have been obvious to one having ordinary skill in the art at the time the invention was made to employ various known gel analyses techniques as a means of optimizing the data, since it has been held that the provision of adjustablity, where needed, involves only routine skill in the art. *In re Stevens,* 101 USPQ 284 (CCPA 1954).

Response to Arguments

Applicant's contend that the cited references do not teach the cyanine dye combinations set forth in the disclosure. This argument was carefully considered and found persuasive. Accordingly, the rejections have been modified to include Sargent P.B. (NeuroImage, 1994, Volume 1, Number 4, pages 288-295) and Luby-Phelps et al. (Biophysical Journal, Volume 65, pages 236-242, July 1993).

Sargent P.B. (NeuroImage, 1994, Volume 1, Number 4, pages 288-295) and Luby-Phelps et al. (Biophysical Journal, Volume 65, pages 236-242, July 1993) teach the preferred embodiments, of the instant specification wherein Cy3 and Cy5 are combined for utility (for example see description of figures on pages 8 and 9 – see example 1 on page 22 – see protein labeling on page 24 and 25 – see gel imaging on page 26).

6. For reasons aforementioned, no claims are allowed.

7. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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